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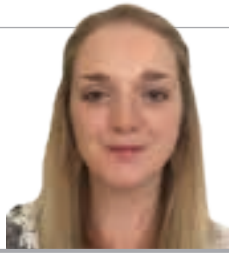
THE ENDOCRINOLOGIST

THE MAGAZINE OF THE SOCIETY FOR ENDOCRINOLOGY

It's time to talk AGEING

Special features
PAGES 6–19

A word from THE EDITOR...



It is my pleasure to welcome you to this issue of *The Endocrinologist*, which (perhaps somewhat ironically for a Spring issue) has the theme of 'ageing'. Ageing is something that remains topical, with UKRI's recent 5-year strategy, 'Transforming tomorrow together', listing 'Securing better health, ageing and well-being' as one of five priority funding areas, with approximately £75 million dedicated to this theme.

Our issue covers a variety of topics in the ageing arena, with articles spanning different aspects of musculo-skeletal and endocrine ageing, and a series of three articles examining various elements of ovarian ageing and menopause.

You'll see that this issue is also brimming with news from the Society for Endocrinology. An interesting article by Deepika Kumanan, Vicky Salem and Kevin Murphy presents the findings of a survey conducted at SfE BES 2021 on equality, diversity and inclusion (EDI). This provides interesting reading on gender balance in audience participation, in terms of posing questions and styles of questions asked (page 30). EDI in article commissioning is something that was discussed at our recent board meeting for *The Endocrinologist*, where we considered how we, as an editorial board, can commission articles from more diverse authors. If there is a topic area or theme in endocrinology that you feel passionately about, and on which you would be willing to contribute an article, please do get in touch with us.

In our interview on page 20 with Márta Korbonits, the new President of the Society, she provides some sage advice. I think it is applicable at all career stages: believe in yourself and your ideas, setbacks are part of the job and reinvent yourself from time to time. Wise words for us all to remember!

With best wishes

KIM JONAS

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The year in review

Become a contributor... Contact the Editorial office at **endocrinologist@endocrinology.org**

The Society welcomes news items, contributions, article suggestions and letters to the Editor. We would also like to hear your feedback on this issue of the magazine.

Deadline for news items for the SUMMER 2023 issue: **30 March 2023**.

Front cover image ©Shutterstock

APPLY FOR THE ESA–SfE EXCHANGE AWARD

The newly launched ESA–SfE Exchange Award will allow you to present your work at the Endocrine Society of Australia's annual meeting, as well as spend time with a research group. This Award provides members of the Endocrine Society of Australia or Society for Endocrinology with up to £4,000 (AU$7,000) towards travel and expenses associated with a research-based placement. The application deadline is 31 March. Discover more at **www.endocrinology.org/esa-sfeexchange**.

esa endocrine society of australia

Society for Endocrinology

Clinical Resource HUB

SHARE YOUR EXPERTISE IN THE CLINICAL RESOURCE HUB

Has your clinic introduced something that has improved your practice?

If the answer is yes, you could improve clinical service delivery and unify patient care by sharing it with the wider endocrine community! We are currently looking for resources related to clinical pathway guides, virtual care, Patient Initiated Follow-Up (PIFU) and patient safety. Log in at **www.endocrinology.org/members** to explore and share.

BE RECOGNISED AS A FUTURE LEADER IN ENDOCRINOLOGY

Apply to join the Society's Leadership and Development Awards Programme to benefit from a wide range of opportunities. These are all aimed at developing your career and professional profile, to help support you as a future leader in our discipline. The 2023 application deadline is 12 April. Visit **www.endocrinology.org/leadership** for more details.

SPREAD THE WORD: YOU AND YOUR HORMONES ON TWITTER

We have launched a You and Your Hormones Twitter account to help achieve our mission of providing students, teachers and the public with accurate information and resources about endocrinology. You could help us to promote reliable endocrine-related resources online by sharing and following our new account at **www.twitter.com/Your_Hormones**.

SUBMIT YOUR PAPERS TO OUR INSULIN AND DIABETES COLLECTION

You have until 31 May 2023 to submit your articles for inclusion in a joint collection between *Journal of Endocrinology* and *Journal of Molecular Endocrinology*. This will focus on the molecular mechanisms behind the development of insulin resistance and type 2 diabetes mellitus.

Learn more on the journal websites: **joe.bioscientifica.com** and **jme.bioscientifica.com**.

HELP IMPROVE SCIENCE REPORTING IN THE MEDIA

Become a Society Media Ambassador to share your expertise with journalists and help them to report more responsibly and accurately on endocrinology-related topics in the news. Find out more at **www.endocrinology.org/engaging-with-the-media**.

ADVERTISE YOUR VACANCIES TO OUR COMMUNITY

Attract the best talent by sharing your job, studentship and grant opportunities with our membership. Check current vacancies at **www.endocrinology.org/careers/jobs**.

WITH GRATEFUL THANKS

We are grateful to the estate of the late Mrs Phyllis Horne Menzies for her £62,000 legacy to the Society during 2021.

SOCIETY CALENDAR

24 March 2023
NATIONAL CLINICAL CASES
London, UK

23 April 2023
THYROID ULTRASOUND
Birmingham, UK

24 April 2023
EMERGING RESEARCH LEADERS
Birmingham, UK

24–26 April 2023
CLINCIAL UPDATE
Birmingham, UK

25–26 April 2023
ENDOCRINE NURSE UPDATE
Birmingham, UK

13–15 November 2023
SfE BES 2023
Glasgow, UK

GRANT AND PRIZE DEADLINES

22 March 2023
PUBLIC ENGAGEMENT GRANT

31 March 2023
ESA–SfE EXCHANGE AWARD

5 April 2023
PRACTICAL SKILLS GRANT

12 April 2023
LEADERSHIP & DEVELOPMENT AWARDS PROGRAMME

26 April 2023
STUDENT VIDEO AWARD

26 April 2023
UNDERGRADUATE ACHIEVEMENT AWARD

3 May 2023
EARLY CAREER GRANT

3 May 2023
EQUIPMENT GRANT

17 May 2023
ENDOCRINE NURSE GRANT

17 May 2023
MEETING SUPPORT GRANT

HOT TOPICS

SOCIETY FOR ENDOCRINOLOGY OFFICIAL JOURNALS

Society members have free access to the current content of *Journal of Endocrinology*, *Journal of Molecular Endocrinology*, *Endocrine-Related Cancer* and *Clinical Endocrinology* via the Members' Area of the Society website, **www.endocrinology.org**. *Endocrine Connections*, *Endocrinology, Diabetes & Metabolism Case Reports* and *Endocrine Oncology* are open access and free to all. Publishing in *Endocrine Oncology* is currently free.

JOURNAL OF ENDOCRINOLOGY

Elucidating serpinA3N's role in non-alcoholic fatty liver disease

Abnormal hepatic lipid metabolism is a major contributor to non-alcoholic fatty liver disease (NAFLD). NAFLD is strongly associated with the development of insulin resistance and type 2 diabetes.

SerpinA3N (serine (or cysteine) peptidase inhibitor clade A member 3N) is a member of the serpin family of proteins, a group of proteins that inhibit serine proteases. It has been shown to play a role in glucocorticoid-induced myopathy, and is upregulated by a high fat diet.

In this paper, Tran *et al.* identify the role of serpinA3N in governing NAFLD progression and glucose homeostasis. They characterise a serpinA3N hepatic knockout, detailing protected glucose tolerance and insulin sensitivity. This model also demonstrates resistance to diet-induced obesity. The study shows, for the first time, that co-ordination of leptin and insulin may, in part, be driven by serpinA3N, and that this protein may have an important role in the manifestation of NAFLD.

Read the full article in *Journal of Endocrinology* **256** e220073

JOURNAL OF MOLECULAR ENDOCRINOLOGY

An adventure in early career academic leadership

Instead of the latest research, we are treated to an invited piece by the Journal's Senior Editor, Tijana Mitić, who is a Society for Endocrinology Leadership and Development Awardee for 2020. In this editorial, she discusses her time as an early career academic, addressing a number of the challenges she faced and providing advice and guidance for those following a similar path.

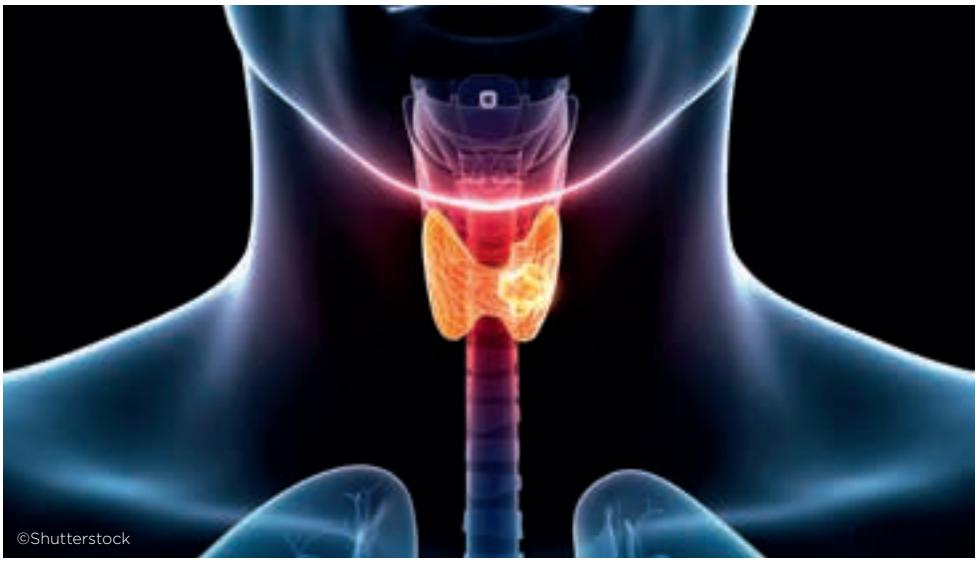
If reading her approach to challenges, such as feeling ready to lead, isn't enough, Tijana uses this platform to point others in the direction of support and help. There is a particularly important section on role models and active participation, which is honest and frank. She concludes by suggesting early career researchers should seek suitable mentors to help push forward with their own careers. Suitable mentors may not be the best performing person in the department, but the one who has found life difficult and made a way through.

Ultimately, this article is a must-read for all academics, regardless of their current position in their careers.

Read the full article in *Journal of Molecular Endocrinology*
doi:10.1530/JME-22-0049


Tijana Mitić

ENDOCRINE-RELATED CANCER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2022 WHO Classification of Endocrine and Neuroendocrine Tumors

The end of 2022 brought with it a very timely review article from Juhlin *et al.* in the area of thyroid tumours. The authors cover the fifth edition of the World Health Organization (WHO) Classification of Endocrine and Neuroendocrine Tumors. This new edition brings in the latest molecular findings in thyroid pathology, to give a new focus on diagnostics and treatments.

With this fifth edition, we see appropriate changes to nomenclature, grading and prognostication of thyroid proliferations, based on pathologic features and molecular profile. It is crucial that endocrinologists and practising physicians who manage thyroid nodules acquaint themselves with this new classification scheme, as tumour entities have been renamed to take into account underlying tumour biology and/or histogenesis, as well as molecular profiles.

Read the full article in *Endocrine-Related Cancer*
doi:10.1530/ERC-22-0293

Hot Topics is written by Sophie Clarke, Craig Doig, Louise Hunter, Gareth Nye and Venkatram Subramanian.

ENDOCRINE CONNECTIONS

Registry for paediatric differentiated thyroid carcinoma within EuRRECa

Paediatric differentiated thyroid carcinoma is the most common endocrine cancer in childhood. Due to its low occurrence, current treatment guidelines are based on small retrospective studies and results in adult patients. In order to achieve a more personalised treatment and effectively reduce complication rates, there is a need for uniform international prospective data collection and clinical trials.

Clement *et al.* report the collection of clinical data by a European paediatric thyroid carcinoma registry for all patients ≤18 years of age with a confirmed diagnosis of differentiated thyroid carcinoma. Data are collected from individuals diagnosed, assessed or treated at participating sites. This registry will be a component of the wider European Registries for Rare Endocrine Conditions (EuRRECa) project which has close links to Endo-ERN, the European Reference Network for Rare Endocrine Conditions. In the future, this may provide the opportunity for research teams to integrate clinical research questions.

Read the full article in *Endocrine Connections* **12** e220306

CLINICAL ENDOCRINOLOGY

COVID-19-related adrenal haemorrhage

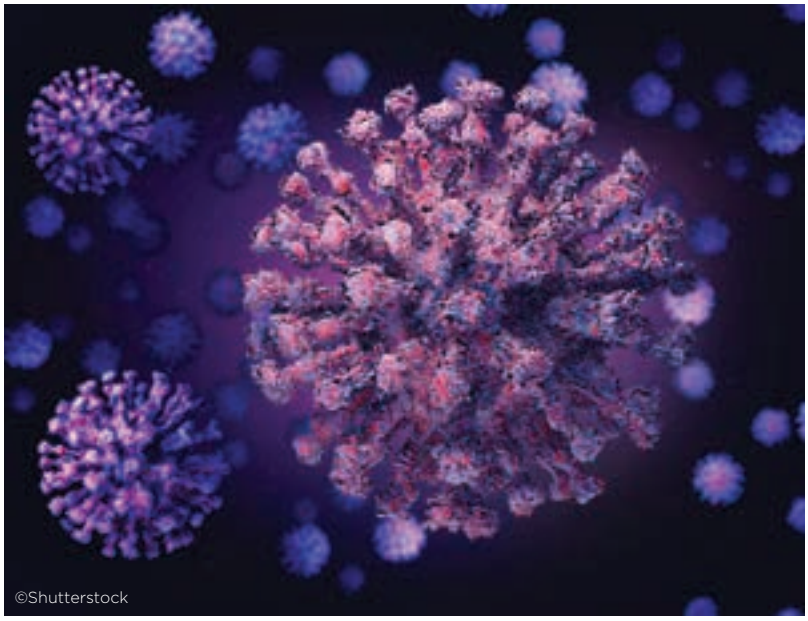
Clinical members of the Society for Endocrinology may recall receiving a survey last year about their experience of patients with COVID-19-related adrenal haemorrhage (AH). The Society's task force that is charged with describing the UK experience of this condition has now collated and reported these data, along with a systematic literature review.

Elhassan *et al.* provide a detailed descriptive summary of the presentations and outcomes of 18 UK patients with either COVID-19 infection-related AH (n=7) or COVID-19 vaccination-related AH (n=11) (the latter being defined by COVID-19 vaccination 5–30 days prior to detection of the adrenal problem). It is of note that most of these patients had a concomitant diagnosis of definite or probable vaccine-induced immune thrombocytopenia and thrombosis (VITT).

AH is thought to be an under-diagnosed condition. This study will therefore make useful reading for both acute physicians and endocrinologists. In particular, the authors highlight acute abdominal pain as a presenting feature, and thus the need to consider this diagnosis in patients with COVID-19 infection, or with COVID-19 VITT, who report abdominal pain.

AH was bilateral in 12 out of 18 patients, and all of these patients required glucocorticoid treatment. The authors therefore suggest immediate, empirical glucocorticoid replacement in bilateral AH, with a low threshold for its initiation in patients with unilateral AH, especially when VITT is present.

Read the full article in *Clinical Endocrinology* doi:10.1111/cen.14881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ENDOCRINE HIGHLIGHTS

A summary of papers from around the endocrine community that have got you talking.


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Outcomes in children whose mothers received metformin for type 2 diabetes while pregnant

Metformin is an insulin sensitiser, increasingly used in patients with type 2 diabetes who are pregnant. However, there are limited safety data available to understand the impact of metformin on the children of women who take it, with some early studies suggesting its use could be associated with increased rates of childhood obesity.

In this study, Feig and colleagues included infants of women who had participated in the MiTy randomised controlled study, where women who had a diagnosis of type 2 diabetes and were pregnant were randomised to receive either 1000mg metformin twice daily or placebo. Infants underwent anthropometric measurements at 3, 6, 12, 18 and 24 months of age.

Of the eligible children, 283 (61%) were included. At 24 months of age, there was no difference in body mass index (BMI) Z-score or mean sum of skinfold thickness between those who had received metformin and those who had not, and metformin use did not predict BMI Z-score.

These data are reassuring with regards to the early health impact of metformin use in pregnancy. However, follow-up studies are required to determine the longer term impact of metformin use in the children of women who are prescribed metformin during pregnancy.

Read the full article in *Lancet Diabetes & Endocrinology* doi:10.1016/S2213-8587(23)00004-9

ASSISTED CONCEPTION AND AGEING

WRITTEN BY KUGAJEEVAN VIGNESWARAN, IPPOKRATIS SARRIS AND SESH K SUNKARA

The relationship between ageing and assisted conception is complex and multifaceted. On one hand, advances in assisted reproductive technology (ART) have made it possible for many couples to conceive later in life. On the other hand, age remains one of the most significant factors determining the likelihood of being able to conceive, either naturally or with the help of ART.

Reproductive ageing refers to the decline in fertility that occurs with increasing age in both men and women, and which is more pronounced in women. In women, reproductive ageing is characterised by a decline in ovarian reserve, in terms of both the quantity and the quality of oocytes. Advancing female age is linked with a decline in fertility and an increased risk of miscarriage.

In this overview, we will focus on some of the aspects pertaining to female reproductive ageing and its impact on natural conception as well as ART outcomes.

FEMALE REPRODUCTIVE AGEING

Ovarian development begins from week 5 of gestation, and the total pool of primordial follicles is formed by the 20th week of fetal life. From this point onwards, there is a progressive depletion of primordial follicles until reproductive senescence, i.e. the menopause.[1]

Although it is thought that approximately 6–7 million primordial follicles are formed initially, only 300,000–400,000 are retained at menarche, and between 400 and 500 follicles reach the ovulatory phase during the reproductive lifespan of healthy women.[2]

As women get older, their chances of getting pregnant naturally decline. Studies that have attempted to model the rate of this decline across populations have shown that, compared with the level observed in women aged 20–24 years, fertility is reduced by 6% for women aged 25–29 years, by 14% for those aged 30–34 years and by 31% for those aged 35–39 years, with a much greater decline thereafter.[3]

OVARIAN RESERVE

Although ovarian reserve has been shown to correlate inversely with age, there can be significant variations in ovarian reserve between women of the same chronologic age.[4]

Ovarian reserve testing refers to the means by which the primordial follicular pool can be determined. Biochemical hormone profiles, including early follicular phase follicle-stimulating hormone and inhibin B levels, can reflect ovarian reserve. However, they are subject to substantial inter-cycle variation. Serum concentrations of anti-Müllerian hormone (AMH), which is produced by early antral follicles, are more stable and potentially reflect the primordial follicular pool size more accurately.[5]

An antral follicle count, which is a ultrasonographic measure of ovarian reserve performed during the early follicular phase, has been shown to be equivalent to AMH in multiple studies.[6]

OOCYTE QUALITY AND EMBRYO EUPLOIDY

Ageing has been shown to result in a decline in oocyte quality as well as in number. This can be demonstrated by the restoration of pregnancy rates seen when older women opt to use egg donation with *in vitro* fertilisation (IVF) treatment, in comparison to pregnancy rates achieved when using their own eggs.

The lower success rates seen in older women undergoing IVF with their own eggs is attributed mainly to the poor quality of the embryos, as well as the increased embryo aneuploidy rate encountered with increasing female age. Aneuploid embryos are embryos with the wrong number of chromosomes, whereas euploid embryos are those with the correct number of chromosomes. According to some studies, the embryo aneuploidy rate is reported to be ~30% in women aged ≤30 years and as high as 85% in women aged >42 years.[7] Embryo aneuploidy is also the main reason for the higher miscarriage rate among older women.

IMPACT ON ART OUTCOMES

The impact of ageing on fertility treatment outcomes is quite evident from ART registries. When examining Human Fertilisation and Embryology Authority data for 2019 birth rates for all women undergoing IVF in the UK, one can observe a clear trend. Comparing fresh IVF cycles only, the birth rate was 32% in the under-35 age group per embryo transfer, 25% for those aged 35–37, 19% for the 38–39 age group and below 5% for women aged 43 and above.[8] Data from the Society for Assisted Reproductive Technology in the USA showed that, in 2019, the percentage of singleton live births per cycle started was 51% for under 35s, dropping to 38.3% in the 35–37 age group, 25.1% in those aged 38–40, and as low as 12.7% for women aged 41–42.5.[9]

FERTILITY PRESERVATION

In terms of therapeutic approaches to mitigate for the decline in female fertility with age, women may opt to undergo fertility preservation via oocyte vitrification.

The use of oocyte vitrification, primarily for social reasons, has seen improvements in the techniques, resulting in improved post-thaw viability, fertilisation and clinical pregnancy rates. The process is still limited, however, by age-dependent oocyte quality and capacity of the ovaries to respond to ovarian stimulation.[10]

CONCLUSION

Reproductive ageing results in a gradual decrease in both oocyte number and oocyte quality. This is evident when one examines the relative success rates of couples undergoing IVF with their own eggs, as there is a clear downward trend in live births associated with increasing female age. The fact that ART may, therefore, not be able to overcome or compensate for reproductive aging, following an infertility diagnosis, is an important message to communicate to all couples who are contemplating their reproductive wishes.

KUGAJEEVAN VIGNESWARAN, IPPOKRATIS SARRIS AND SESH K SUNKARA
King's College London and King's Fertility, London

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PREMATURE OVARIAN INSUFFICIENCY

WHICH HORMONAL THERAPY SHOULD WE CHOOSE?

WRITTEN BY ZACHARY NASH AND MELANIE DAVIES

Loss of endocrine function of the ovaries, with resultant absolute deficiency of female sex steroids, is typically associated with ageing. If this happens before the age of 40 years, this is defined as premature ovarian insufficiency.

The prevalence of POI is around 1–3%.[1] In most cases, the cause of POI is unexplained. Around 30% of patients will have an underlying genetic condition, with Turner syndrome and Fragile X being the most common. Other cases are associated with gonadotoxic chemotherapy or radiotherapy, or surgery for malignant or benign disease. Almost all female patients with galactosaemia will have POI.

Women with POI present with primary or secondary amenorrhoea; primary amenorrhoea is more common in those with a genetic cause. A diagnosis of POI is made based on menstrual disturbance (absent or infrequent irregular periods) and follicle-stimulating hormone (FSH) being raised beyond physiological levels (>25–30IU/l) on two occasions, taken a minimum of 4–6 weeks apart.[2] In a minority of cases, the diagnosis will be self-evident, with a history of surgical removal of both ovaries.

NICE,[3] the International Menopause Society,[4] the European Society of Human Reproduction and Embryology[2] and the British Menopause Society[5] have all published guidelines covering the diagnosis and management of POI.

'The POISE Trial aims to find the relative effectiveness of HRT (any route) compared with the combined oral contraceptive.'

HEALTH IMPACT OF POI

Untreated oestrogen deficiency has a significant impact on quality of life. Most women report bothersome menopausal symptoms including hot flushes, sleep disturbance, mood disturbance, or vulvo–vaginal dryness and discomfort.

Epidemiological studies have also consistently shown an association between untreated POI and increased risk of osteoporosis and fracture[6] and heart disease.[7] One cohort study of women with surgical menopause has even shown an association with cognitive impairment and dementia.[8]

CHOICE OF HORMONE THERAPY

All guidelines recommend treatment with either hormone replacement therapy (HRT) or the combined oral contraceptive (COC) until the average age of natural menopause (51 years of age) to maintain health.[2–5]

Although POI is associated with infertility, around 5–10% of women with POI can conceive spontaneously, due to fluctuating ovarian activity. If contraception is needed, the COC inherently provides contraceptive cover. Alternately, an HRT regimen incorporating the Mirena coil or with the addition of the progestogen-only pill can be used.

The COC is often seen as more acceptable to young people and is free of prescription charges. It is recommended that a COC with 30µg ethinyloestradiol and progestogen is prescribed as an extended regimen (tricycling for 63 days followed by a 4–7 day interval, or flexible extended use, taking it continuously with breaks of 3–4 days if breakthrough bleeding occurs). Using the COC in these ways minimises the number of days without oestrogen exposure.

HRT is generally prescribed in secondary care and comes in a variety of formulations with different routes, doses and commercial availability. The recommended daily dose of oestradiol for POI is not less than 2mg orally, a 50µg patch or 1.5mg gel. This dose can be titrated upwards if needed for symptoms or to maintain bone density.

Women should be reassured that, unlike HRT use after the average age of menopause, the incidence of breast cancer is not higher than that of the general population in those using HRT <40 years of age.[9]

Little evidence is available to support patients and clinicians in choosing between HRT and the COC to maintain health.

A small randomised controlled trial suggests that blood pressure is lower in HRT users than in COC users;[10] however, the clinical significance of this in isolation is unclear. A larger randomised controlled trial suggests that bone mineral density is higher in HRT users than in COC users,[11] but this alone has not been sufficient to change practice.

Adding testosterone to adequate HRT does not appear to further increase bone mineral density (BMD), and its use should be restricted to cases with POI and low sexual desire who are seen in a specialist setting.[2]

POISE TRIAL

The POISE Trial (**www.poise.ac.uk**) is funded by the NIHR Health Technology Assessment Programme. It aims to find the relative effectiveness of HRT (any route) compared with the COC in individuals with POI.

The primary outcome is the absolute BMD (g/cm^2) of the lumbar spine at two years from randomisation, assessed by a dual-energy X-ray absorptiometry scan. Secondary outcomes include menopause-specific

Table. POISE Trial eligibility criteria.

Inclusion criteria	
1.	Diagnosis of POI (based on NICE guidelines)
2.	Will be aged ≥18 years up to <40 years at randomisation
3.	Not intending to become pregnant within 12 months
4.	Not taken any HRT or COC treatment for the last four weeks or willing to stop HRT/COC treatment for a minimum period of four weeks prior to randomisation
5.	Must provide written/electronic informed consent
Exclusion criteria	
1.	Contraindications to HRT or COC
2.	Taking other drugs affecting BMD, e.g. bisphosphonates and long term use of systemic corticosteroids (dietary supplements, e.g. vitamin D, calcium and short course of corticosteroids are permitted)
3.	Receiving sex steroid hormones for puberty induction
4.	Participation in a clinical research study (currently or in the last three months) involving testosterone treatments or novel HRT formulations

quality of life, sexual function, work productivity, and satisfaction with treatment. In a small number of sites, participants are asked to provide blood and urine samples for biomarker analysis. Consent is also obtained for long term follow up using routine data.

With support from The Daisy Network, a charity for women with POI, and the Turner Syndrome Support Society, the POISE Trial aims to recruit 480 women with POI across 24 centres around the UK. Recruitment began in June 2022 and will continue for 36 months. The POISE Trial eligibility criteria are outlined in the Table on page 7.

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MAKING SPACE FOR MENOPAUSAL EXPERIENCES

WRITTEN BY NALINI KAUSHIK AND VIKRAM TALAULIKAR

Menopause, as an issue, lies at the intersection of gender, sex, reproduction, ageing, public health and economy, affecting millions of individuals worldwide. For many, menopausal transition can be associated with unpleasant symptoms and physical/psychological changes that negatively impact quality of life and have implications for long term health. Some may face discrimination and exclusion at social and economic levels at this stage of life.

There has been a significant recent focus in the media on menopause and the difficulties of living through the menopausal transition for some individuals, with its impact on quality of life and work productivity. This presents an opportunity to create more awareness of menopause-related health and quality of life. However, more work needs to be done to address inequalities that exist in relation to access to evidence-based healthcare, as well as workplace and social support for women across various sociocultural backgrounds and for transgender, non-binary and gender-fluid individuals.

AN UNMET NEED FOR EDUCATION

The prospect of going through the menopause provokes anxiety and uncertainty for many individuals. There remains a lack of educational framework or resources that can help prepare them for what is to come. Many individuals under 40 years of age have limited education regarding the menopause.

That limited education for women and their general practitioners is causing perimenopausal women to go through this stage in their lives without knowledge and appropriate medical care is a case in point.[1,2] Instead of looking at this time in one's life as a new and natural phase, many menstruating individuals get redefined in terms of loss of fertility, loss of femininity, an altered role in the family and a change in societal status.

'It seems pertinent to change the negative narrative around the midlife phase of a menstruating individual, to one which is not tied to ageist and sexist stereotypes.'

ADDRESSING INEQUALITIES

Currently, in UK law, menopause is not a specific protected characteristic under the Equality Act 2010 which protects workers against discrimination. However, as per the Health and Safety at Work Act 1974, an employer must, where reasonably practical, ensure everyone's health, safety, and welfare at work. Employers are encouraged to have workplace policies in place that support staff affected by menopause.

There are several factors that play a role in health inequalities related to menopause. First, the majority of global research and clinical care infrastructure remains focused on women's well-being in relation to reproductive health concerns and unique requirements of adolescent and fertile women. There is a need for more research funding and investment of clinical resources in healthcare related to perimenopause and menopause.

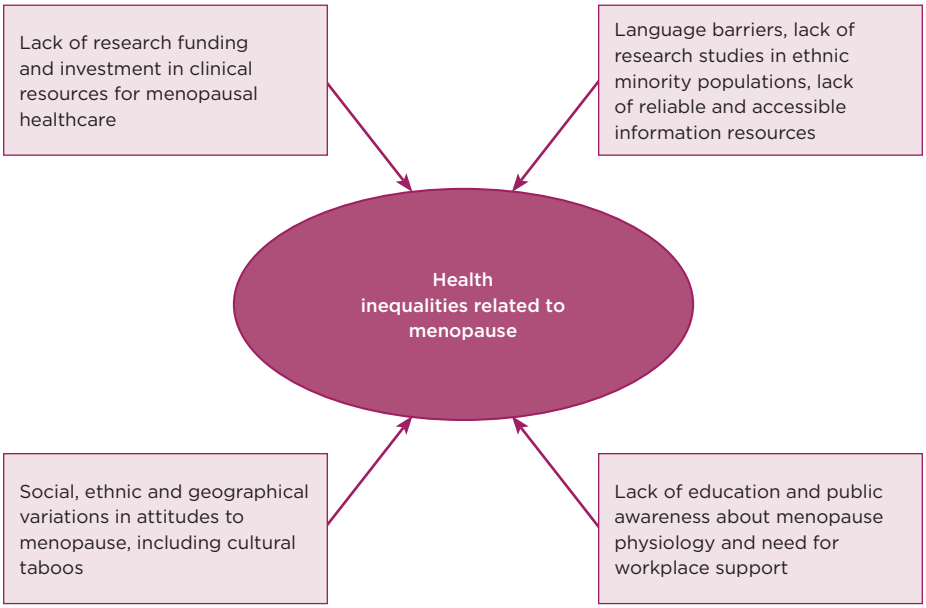

Figure. Factors affecting health inequalities related to menopause.

Furthermore, there are biological variations in age at menopause and severity of menopausal symptoms across ethnicities. Studies show that women of colour tend to enter perimenopause and menopause at earlier ages than their white peers, have longer transition periods, and experience more intense hot flashes and vaginal symptoms.[3] Current healthcare systems do not sufficiently address menopause-related issues that are specific to different ethnicities, and there remain barriers related to language, access to information and cultural taboos in seeking health advice. Research on menopause is also largely focused on the white population. These factors underpin the need to improve participation from other ethnicities as well as transgender individuals.

SOCIETAL ISSUES

Societal attitudes and sociocultural perceptions can affect how individuals perceive and manage their menopausal symptoms, and these can vary significantly.

For instance, in some rural villages in India, Iran and Africa, where fertility and having large families are highly valued, women may fear, as they reach menopause, that their husbands might abandon them for younger women and that they might face exclusion.[4]

There has been an evident shift in women's participation and contribution to the global economy. This also means that a growing number of women aged 45 years and older participate in the labour market, making menopause an integral part of working individuals' lives. However, despite their significant economic contribution, a parallel trend has been the impact on an individual's career projection in the menopausal years, with significant menopause-related productivity losses and negative experiences in the workplace due to menopause.[5]

Importantly, menopause is not experienced exclusively by women; rather, trans men, trans women and non-binary and gender-fluid individuals also experience menopause. However, hitherto, menopause literature is largely framed around the experiences of cisgender women, with transgender individuals receiving little or no guidance about what happens when they reach the age when women typically go through menopause.

In one study, transgender women expressed uncertainty regarding clinical management approaches at and beyond the menopausal age, as well as for those beginning hormone replacement therapy at this age. This ambiguity reflects the lack of consensus on hormone therapy management within healthcare provision and the lack of empirical evidence relating to long term effects after the age of 50.[6]

CHANGING THE NARRATIVE

It seems pertinent to change the negative narrative around the menopause, to one which is not tied to ageist and sexist stereotypes. Greater menopause awareness among all individuals will help tackle negative notions around menopause and help build constructive responses towards transitioning human physiology. Such awareness can be achieved by means of an educational curriculum starting from school, public health awareness campaigns, workshops, programmes, literature in different languages, involvement of ethnic/transgender groups and workplace policies.

Workplace menopause policies and support for individuals experiencing difficulties during menopause will ensure help for the quickest growing workforce demographic. The ability to retain these workers would greatly benefit the employee, employer and economy.

The current gaps in the discourse around menopause necessitate awareness and education for all individuals, particularly medical professionals and menstruating individuals themselves, so that equitable and inclusive healthcare becomes a reality.

DISCLAIMER

The term 'individuals' is used to identify all who experience menstruation as well as menopause.

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MUSCULOSKELETAL AGEING IN THE WORLD OF ENDOCRINE DISEASE

WRITTEN BY GARETH NYE

Within the UK and most developed countries, we can categorically define our population as an ageing one. Current data suggest around 11 million people (19% of the population) are aged over 65, with this increasing to 13 million over the next decade.

Despite the average person living longer, the years for which we could expect to live in 'good health' have decreased to 62.4 years for men and 60.9 years for women. What these numbers tell us is that almost a fifth of the UK population is living in poor health due to age.[1]

Everyone faces an inevitable decline in their musculoskeletal health with increasing age, and this decline is heavily linked to poor health and disability. As patients with endocrine disease enter the later stages of life, they are more at risk of complications, particularly with musculoskeletal conditions. It is clear that, by focusing on age-related conditions, we could not solely extend lifespan, but increase health span for these individuals (Figure 1).[2]

COMMON MUSCULOSKELETAL AGEING PATHOLOGIES

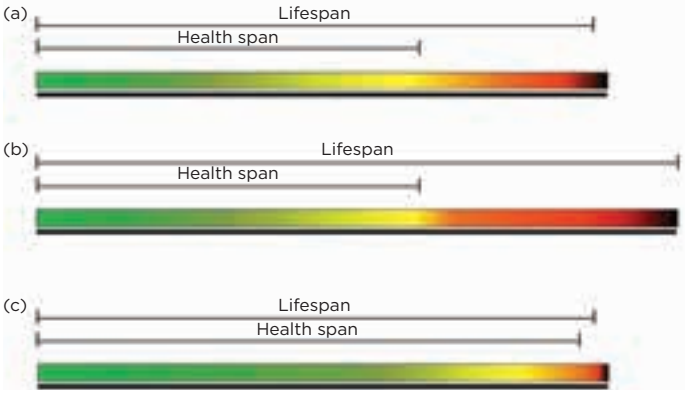
Broadly, age-related changes to our musculoskeletal tissues can fall into three categories:

- muscle-based decline, called sarcopenia
- bone-based decline, usually related to osteoporosis, and
- joint-based conditions, such as arthritis.

All of these conditions are inevitable to some degree, and everyone will suffer functional decline with increased age. Despite this, little progress has been made to counteract the loss. We can see the influence a loss of musculoskeletal function has for the whole-body system in Figure 2. For patients with underlying co-morbidities, the loss occurs to a higher extent and earlier in life, and therefore it is crucial to understand the impact of musculoskeletal loss here.[3]

In this article, I will focus on the impact endocrine diseases play in sarcopenia. Recent reviews of other conditions are available.[4,5]

Figure 1. Differing approaches to treating populations of increasing age. Colours represent the relative health of an individual (green = good health ranging to dark brown = poor health). (a) The normal lifespan of an average person with reported years of poor health and disability. (b) A medical focus on lifespan extension only. (c) A medical focus on extension of health span only.[10]



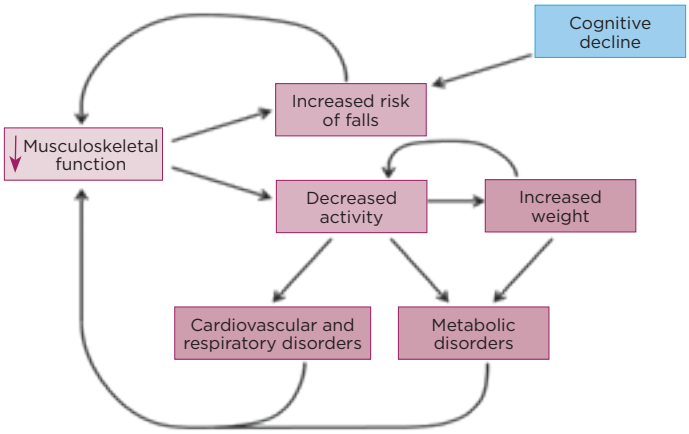


Figure 2. Placing musculoskeletal decline at the centre of age-related health decline. The decrease in musculoskeletal function can lead to increasing falls and decreasing activity, which feedback directly and indirectly, causing further declines. These effects are known to influence other age-related conditions and co-morbidities.

SARCOPENIA

Sarcopenia is characterised by age-related decline in muscle mass and function. By the time a person reaches their 80s, they will have lost approximately 50% of their muscle mass.[6] As muscle mass represents 60% of total body mass, this loss is clearly detrimental to each individual through reduced locomotion, strength and co-ordination, as well as alterations in metabolic processes.

Currently, the only way to avoid functional decline is to ensure you have developed more muscle mass in earlier life to hold off the functional deficit for longer. Treatments have focused on preserving the level of muscle mass a patient has through resistance training and diet, but this obviously doesn't stop the decline.

> *'Use of HRT in the initial postmenopausal period results in significant increases in muscle stem cells, strength and mobility.'*

We have seen in particular endocrine-related conditions that sarcopenia can be exacerbated. Potentially by studying these conditions, we can work backwards to understand the point of functional decline. At the very least, we can identify those groups that are more at risk of functional loss.

ENDOCRINE DISEASES AND SARCOPENIA

Sarcopenia has been described as a new complication of patients with type 2 diabetes, attributed in part to better care and management of the diabetes itself. In these patients, loss of muscle mass and function occurs earlier than in non-diabetic counterparts, with evidence of a decline in patients in their 50s and 60s. Type 2 diabetes is also strongly linked to increased frailty, disability and mortality.

Ultimately, the more muscle mass that is lost in diabetic patients, the less capacity they have to dispose of glucose. In clinic, this would present as a higher glycated haemoglobin value (>8.5%) with decreased muscle mass. Whether the loss of muscle mass comes first, or the diabetes influences the reduction of muscle mass, is not currently known. However, it is clear that,

in our older population of diabetics, special attention should be paid to any presentation of sarcopenia (Figure 3).[7]

Cushing's syndrome is clinically defined by muscle weakness. Glucocorticoids have been shown to influence muscle structure through a loss of type II muscle fibres. Excess cortisol has additionally been shown to impair muscle protein synthesis and mitochondrial function. Despite studies showing that muscle and fat levels were similar in comparison groups, patients with Cushing's syndrome display far less muscle function, due to higher levels of fat infiltration into the muscle tissue. This functional loss can last for more than two years after treatment, which can be highly detrimental in populations already displaying loss of muscle mass and function.[8]

Thyroid hormones have a role in the regulation and expression of over 600 genes in muscle tissue, through their involvement in energy production and metabolism. The presence of hyperthyroidism increases the turnover of protein in muscle tissues, ultimately leading to loss of muscle mass. A number of studies have shown high levels of muscle mass decline and loss of strength in patients with hyperthyroidism.[8]

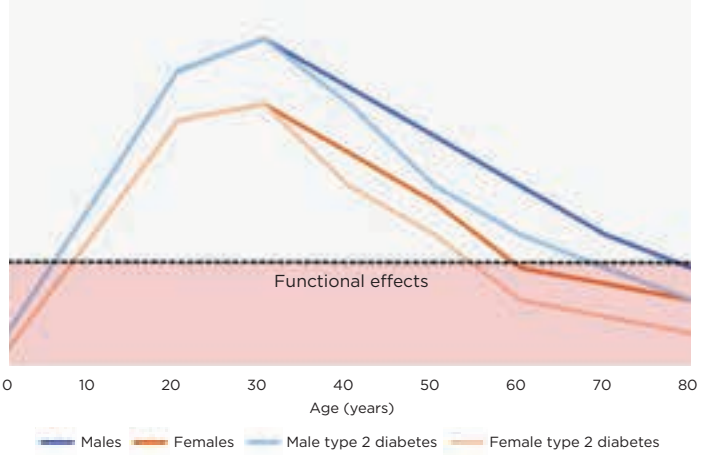
In just these few examples, it is clear that recognising the development of sarcopenia in patients with underlying endocrine conditions is of huge importance for that patient's long term health and well-being. Although we may not be able to prevent the decline in mass and function, we can look to commence suitable treatments in these populations earlier, to ensure function is maintained for as long as possible.

SARCOPENIA AND THE MENOPAUSE

The incidence and impact of musculoskeletal conditions are highly sex-specific. Sarcopenia is intimately linked with the female ageing process. One of the most influential times in a women's life is when she reaches the menopause, which brings about huge physiological change, particularly in endocrinology.

One of the more potent hormonal changes that is displayed is in the levels of the oestrogen hormone oestradiol. This hormone is involved in the regulation of the menstrual cycle and in the development of female sexual characteristics but is relevant to muscle, as muscle fibres contain specific receptors for oestradiol. Oestradiol therefore has a role in muscle function, specifically in stimulating the muscle stem cells to grow and divide, to promote muscle growth.[9]

Figure 3. Representative graph displaying the expected pattern of functional changes in skeletal muscle with increasing age for patients with and without type 2 diabetes. Any value below the functional effects line would probably display in patients as poor mobility or strength.



'Individuals with endocrine disease should be monitored for evidence of musculoskeletal decline, to prevent the early onset of loss of functionality which, in turn, can negatively impact their conditions.'

Without oestradiol present in the system, muscle cells will be unable to repair and replace damaged fibres. Over time, this leads to a culminative loss of mass and function at an accelerated rate. In this situation, we do see some slowing down of the muscle loss with hormone replacement therapies (HRT), but its power comes from quick implementation. Use of HRT in the initial postmenopausal period results in significant increases in muscle stem cells, strength and mobility when compared with HRT introduced in a delayed postmenopausal period.

The ongoing debate on the risks associated with HRT will prevent this from being a universal approach to sarcopenia but, if we can focus on commencing HRT as soon as possible in those who are suitable, we can begin to make a substantial difference to people.

SUMMARY

Sarcopenia, as with other age-related musculoskeletal diseases, is inevitable for all of us. However, for those with underlying conditions, such as the ones discussed, it can develop sooner and have a greater impact on the individual.

Individuals with endocrine disease should be monitored for evidence of musculoskeletal decline, to prevent the early onset of loss of functionality which, in turn, can negatively impact their conditions.

Simple advice and education regarding the conditions, and introducing resistance exercise and nutritional approaches, may well make the difference. However, as our ability to treat and manage endocrine disease improves, we may soon be faced with a range of age-related effects of endocrine disease that we have never considered before.

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TYPE 1 DIABETES
FRAILTY AND COGNITIVE DECLINE

WRITTEN BY AMAR PUTTANNA

The management of type 1 diabetes (T1DM) has traditionally focused on the younger individual, partly due to the long-held consideration that this autoimmune disease will present in a younger cohort. Even key trials (such as the Diabetes Control and Complications Trial; DCCT) tend to have a younger cohort, making generalisability to older populations difficult, leading to a relative dearth of high quality evidence in this cohort.

Though the peak age at which T1DM is diagnosed is relatively young, it is known that it can and has been diagnosed across a broad age range, with prevalence highest in those who are 35–60 years of age.[1] The number of people older than 65 years with diabetes has been projected to reach 195.2 million by 2030 and 276.2 million by 2045.[2]

Additionally, with greater awareness and priority focus in national frameworks, as well as therapeutic and management options for care, more and more people with T1DM are living longer. This highlights the need to consider the older adult with T1DM, and the management of diabetes in settings of more common co-morbidities in this age group, such as frailty and cognitive decline.

'Diabetes has been shown to be a risk factor for the development of frailty, and there is some evidence suggesting that improved glycaemic control may reduce the severity of frailty.'

FRAILTY

Traditional definitions of 'old' based on chronology have long been discarded, as we are all aware that 'age is but a number' and does not define the individual. This is where the concept of frailty has gained prominence. Frailty is defined as 'a distinctive health state related to the ageing process in which multiple body systems gradually lose their in-built reserves'.[3] It is important to recognise frailty, because it has been shown to increase the risk of poorer health outcomes, including hospitalisation and mortality.[4]

In the setting of diabetes, there is a paucity of data looking at those with T1DM and frailty. There is more evidence in the setting of type 2 diabetes (T2DM), given the older cohort. Diabetes has been shown to be a risk factor for the development of frailty, and there is some evidence suggesting that improved glycaemic control may reduce the severity of frailty. However, the key intervention has been shown to be exercise, specifically resistance training.[5]

Recent changes to guidelines highlight the need to consider several factors when examining targets in those with frailty, and adapting the 'individualised approach' so often mentioned in the management of people with diabetes. There have also been consensus discussions on frailty and intensification and de-escalation of therapy. However, these tend to focus on T2DM.[6] The management of T1DM in this setting, though following similar principles, tends to be limited, due to the need for insulin therapy. Considerations around hypoglycaemia reduction, by reducing insulin requirements but not cessation of therapy, are key to avoiding hypoglycaemia risk, without increasing the risk of rebounding hyperglycaemia or diabetic ketoacidosis.[7]

COGNITIVE IMPAIRMENT

Another important area to consider is the development of cognitive impairment in those with T1DM. Diabetes is an established risk factor for dementia, with a roughly twofold increased risk.[8] There are many possible reasons for the link between diabetes and dementia. Vascular disease and cerebral ischaemia, as well as a higher risk of stroke, could lead to cognitive impairment as, indeed, does exposure to higher levels of glycated

haemoglobin (HbA1c). It may be argued that cognitive impairment is a chronic complication of diabetes.

Hypoglycaemia is an interesting and important consideration in the setting of cognitive impairment. There has been conflicting evidence as to whether hypoglycaemia is causative of chronic cognitive impairment, with the DCCT–Epidemiology of Diabetes Interventions and Complications (EDIC) Trial showing no worsening of cognition in those with severe hypoglycaemia (SH) over an 18-year follow up. This was superseded by a 32-year follow up, which revealed that higher exposure to HbA1c and SH was linked to poorer cognitive scores.[9] Further data in T1DM from the Study of Longevity in Diabetes (SOLID) Study also showed that SH was associated with poorer cognition.[10]

'The number of people older than 65 years with diabetes has been projected to reach 195.2 million by 2030 and 276.2 million by 2045.'

This lends further support for why SH (and hypoglycaemia in general) should be avoided both in older adults, to prevent cognitive decline, and also in those with cognitive impairment, to prevent worsening cognition. The situation is complicated by the fact that many will be unable to recognise hypoglycaemia, nor will it be identified, due to the difficulty for third parties of recognising the change in baseline/confusion. A higher index of suspicion and education is therefore warranted.

FUTURE CONSIDERATIONS AND IMPLICATIONS

Given the challenges in clinical management and the historically limited evidence base, it is imperative that older adults with T1DM are considered in future guidelines, policies and research studies.

Practically, whilst the use of technology has been well established in many areas, the opportunities for the use of continuous glucose monitoring systems in frail older adults or those with cognitive impairment need further exploration. The presence of hybrid closed loop systems also invites consideration of whether stricter glycaemic control without increasing hypoglycaemia risk might result in changes to glycaemic targets in older adults.

Beyond this, research around appropriate targets, multimorbidity and complication risk in older adults would aid understanding and support of those in this group.

As can be seen, the importance of understanding how management differs and the clinical considerations for older adults is paramount for all those who care for people with diabetes, especially those with T1DM. Given the longer modern life expectancy, healthcare professionals and systems need to proactively learn and plan for this.

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NEVER THE TWAIN SHALL MEET ...BUT WHY NOT?

WRITTEN BY MARY MURPHY

Mary Murphy and her son both live with type 1 diabetes. Here, Mary reflects on her differing experiences of care of individuals with the condition between adult and paediatric services.

Ask any diabetes specialist about how they deliver their service today, and they will tell you that they wish they could do better for their cohort: paediatric or adult. As an adult who has had type 1 diabetes for 25 years, diagnosed as an 18-year-old, and now also a parent of a teen with type 1 diabetes, diagnosed when a little 6-year-old, I continuously compare the services.

Through the eyes of a user of an adult service, paediatric services are trying their best to support and treat the whole type 1 diabetes 'iceberg'. They see the diabetes part, the numbers that define our medical state, and assess our bodies for complications. But they also know to give access to technologies that help improve health outcomes today, so our children can 'be on an equal playing field' at school, as well as to listen to the person who has the condition, and the carer who is the 'force' that tries (imperfectly) to bring all this together (this is the bit of iceberg that is below the water). They try to help find solutions to manage the things in life that make this already difficult, chronic condition, less so. Their resources are still limited, but they continue to push for what is needed.

In adult services, I feel the delivery and support are provided differently. Being diagnosed in an adult clinic, I looked very different to the others in my waiting room. I didn't know any better though than to assume (and fear) that my potential destination was the same as all who, unfortunately, have diabetes. Until recently, I hadn't gained access, through perseverance and grit, to any technologies to help me to look after myself more easily. With these now in my life, and knowing the effort I had to make to advocate for myself, I ask 'Why is this necessary?' I am led to believe, based on lack of access, that I am an outlier, that others with type 1 don't need diabetes technologies and manage well without. Peer support tells me otherwise.

With the same support, access to and choice of technologies as paediatric patients, to help us self-manage this condition AND live our busy lives, our potential health destination is not the same as that of the whole diabetes community. We even have the potential to have healthier outcomes than our non-diabetic peers.

What should a service for all who have type 1 diabetes look (and feel) like? I am happy to say that, by volunteering as a service user in the Northern Ireland (Adult) Diabetes Network over the last few years, I have seen what this can look like, on paper, for adult services. It sounds very similar to paediatrics today. More appointments, more choice, more opportunities to talk about management and inter-references, but also psychological support. However, the reality on the ground, right now, is very far from this.

Why is it like this? Does the burden on our lives of having type 1 diabetes not need this support for better health outcomes, like it does in paediatrics? Do we not deserve to have the whole of the type 1 iceberg supported too? The huge, invisible burden of self-managing this condition doesn't disappear as we grow older.

Clinical care for diabetes focuses on numbers and on treating complications, and holds the keys to our best self-care. Why treat us as diabetes numbers and forget to also support us along our personal journey, with the biggest part of managing type 1? Programming out potentials for worse health outcomes in care pathways is wonderful, but you can't programme out some types of diabetes. Having any diabetes is so hard, unfair, and not the person's fault. Treating all who have diabetes as one type, by just looking at numbers, causes so many other things to manifest. It forces the strong with type 1 to educate themselves and to take hold of their own management but, in turn, this penalises them through lack of access to technologies.

> ***'If we always do what we've always done, we'll always get what we've always got.'***

Others will advocate for better support and for type 1 diabetes to be seen and its burdens validated. But does this advocacy for better care for type 1 cause harm and shame in our community to those who have type 2 diabetes or any other type, for instance? Should we stop advocating for the care we need? Is treating just diabetes numbers in healthcare the root cause of all this?

See us as you see yourself and your own passions for a long, fulfilling and healthy life; these are ours too. With the right support and technologies, people who have type 1 diabetes are not automatically destined for serious diabetes complications. But having these technologies doesn't magically make our diabetes disappear. Look to paediatrics to learn how they are ever-improving their care for children who have type 1.

If we always do what we've always done, we'll always get what we've always got.

MARY MURPHY

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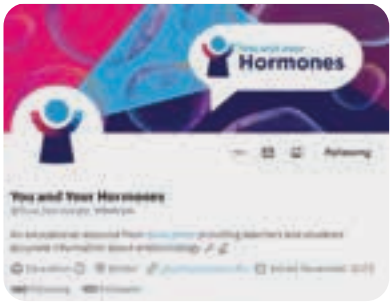

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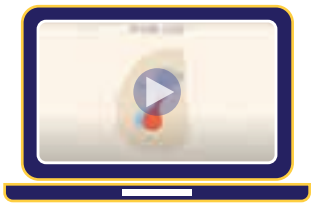

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AGEING: THE ROLE OF OXIDATIVE STRESS AND MITOCHONDRIA

WRITTEN BY GABRIELE SARETZKI

FIRST PUBLISHED IN ISSUE 130 (2018)

The ageing process is complex and its detailed mechanisms are not yet well understood. However, cellular senescence might play an important role.

WHAT IS SENESCENCE?

Cellular senescence in its various forms – replicative, premature or oncogene-induced – is a stress response.[1] Senescence is an irreversible growth arrest. However, post-mitotic cells can also become senescent, although without the growth arrest feature.[2]

Replicative senescence is best characterised in human somatic cells such as fibroblasts by a continuous telomere shortening.[3] However, telomere shortening can be accelerated by increased oxidative stress[4,5] and thus has immediate significance for the ageing process, where telomeres are thought to be a possible biomarker.[6] However, this is often just related to average telomere length while there is large heterogeneity between individual telomeres,[7] a dynamic regulation of telomere homeostasis by telomerase and TERRA telomere transcription products[8,9] and, most importantly, there can be DNA damage in telomeres without shortening.[10,11]

The direct association between senescence and the ageing process has been demonstrated by ablating these cells from an organism, either genetically[12] or by using senolytics.[13] López-Otín *et al.* have provided a comprehensive characterisation of the ageing phenotype.[14]

THE ROLE OF MITOCHONDRIA

Most oxidative stress within cells is generated by mitochondria. Mitochondrial dysfunction and increased reactive oxygen species (ROS) are features of senescent cells which can be ameliorated with uncouplers and ROS-scavenging agents.[15]

Paradoxically, mitochondria seem to be essential and required for senescence induction, while ablating them prevents senescence and associated features such as DNA damage and senescence-associated secretory phenotype (SASP).[16]

During senescence and ageing, there is an accumulation of pathological mitochondrial mutations while the mutation numbers do not increase.[17] Importantly, there is a certain threshold of around 70–80% of mutated mitochondrial DNA molecules before a phenotype appears.

ROS are thought to be an important source of mitochondrial mutations. ROS are generated at different sites in the electron transport chain, in particular at complexes 1 and 3 during normal physiological functioning of mitochondria.[18] There is also a reverse electron flow back from complex 2 to complex 1.[19] Paradoxically, in some lower organisms, such as worms and flies, it has even been shown that lowering mitochondrial ROS results in a decrease in organismal lifespan.[20,21] It is known that ROS also have important signalling functions,[22] so that complete scavenging of ROS has a rather detrimental effect for mitochondria, cells and organisms.

Recent discoveries show the presence and function of mitochondrial micro RNAs regulating mitochondrial oxidative phosphorylation,[23] and of hormone-like mitopeptides, such as humanin, which are involved in regulation of cellular energetics, insulin sensitivity and glucose homeostasis.[24]

THE RELATIONSHIP WITH AGEING

An important research topic is the relationship between oxidative stress, mitochondria and ageing. It has long been known that ageing is associated with a low level, chronic inflammatory process[25] and low level inflammation seems to correlate best with longevity in humans.[26] Inflammation is also a prominent feature of many age-related diseases.[27]

'Dysfunctional mitochondria activate inflammation as well as senescence, and can stimulate the innate immune response. Thus, their role and that of cellular oxidative stress remains an important field of research.'

To some extent, SASP, which results in a lot of secreted pro-inflammatory molecules,[28] might contribute to the process of inflammation and so-called 'inflammageing'.[25] Via dysfunction and ROS production, mitochondria directly contribute to SASP and senescence.[15]

Baker *et al.* have demonstrated in a senescence clearance mouse model that not only were life- and health span increased, but also that expression of inflammatory genes was decreased upon removal of senescent cells in various tissues, including heart, muscle and kidney.[12]

While the master inflammation regulators nuclear factor-κB (NFκB) and interleukin-1α were thought to be responsible for SASP,[29] a new concept regarding a specific mitochondria-driven SASP has been presented (mitochondrial dysfunction-associated senescence or MiDAS).[30] This, however, remains controversial amongst researchers working on ageing.

Nutrients and glucose stimulate signalling processes in senescent cells, such as the mTor and NFκB pathways.[31,32] NFκB has been shown to modulate oxidative phosphorylation via p53.[33] Consequently, a lack of mitochondria reduced the inflammatory signalling in a cell model.[16]

Another type of inflammation can be induced during cellular injury and leakage of mitochondrial DNA and other components, such as cardiolipin, out of mitochondria. This process can activate damage-associated molecular patterns via pattern recognition receptors.[34] Activation of toll-like receptors (TLR9)[35] and cytosolic DNA sensors such as cyclic GMP–AMP synthase (cGAS)[36] by mitochondrial DNA may be a result of the evolutionary origin of mitochondria and their resulting similarity to bacteria. In addition, ROS resulting from mitochondrial dysfunction can activate the inflammasome[37] while inflammation, in turn, is able to induce senescence in neighbouring cells due to the so-called 'bystander effect'.[38,39]

IN CONCLUSION

In summary, it is fair to state that mitochondria play an important role in the induction of senescence as well as in ageing. New mechanisms are constantly added regarding the detrimental role of excess ROS generated during ageing and senescence. Dysfunctional mitochondria activate inflammation as well as senescence, and can stimulate the innate immune response. Thus, their role and that of cellular oxidative stress remains an important field of research, while the prevention of senescence using senolytics and senostatics has already reached a translational state.[40]

GABRIELE SARETZKI
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Meet your **NEW PRESIDENT**

Márta Korbonits MD PhD DSc FRCP is Professor of Endocrinology and Metabolism at Barts and the London School of Medicine and Dentistry, Queen Mary University of London. Her tenure as President of the Society for Endocrinology began in November 2022 at our AGM. Here, she talks to us about her career, her hopes for her presidency, and her advice for aspiring endocrinologists.

Please tell us about your early career

I am a clinician who has always been interested in science and research. I undertook my first research project during my undergraduate years, and my first job after graduation was actually in research and teaching at a university. When I moved to the UK, due to the regulations around medical licences at the time, I could initially only work in research. While I felt at that point that this was a huge disadvantage, I enjoyed the warm support of Professors Michael Besser, Ashley Grossman and Peter Trainer and, ultimately, this academic grounding really helped me to develop as a clinician scientist and prepared me for the wonderful combination of the clinical and academic aspects of medicine.

Once I was able to join in with clinical work, I started with clinical trials and completed first an MD and then a PhD. Putting together my lab results and the clinical study results, I was lucky enough to get an intriguing set of translational data under my belt. Armed with these, and a bit of courage(!), I applied for an MRC Clinician Scientist Fellowship, which was a major step in my career and created a real opportunity to be a clinical academic. I have carried on with this ever since. And, 20 years later, when I was a member of the same MRC Fellowship Committee, I could really feel the weight of the career-changing decisions that were made there.

What is your specialty?

The first project I found myself working on, here in the UK, was related to the regulation of growth hormone. As it turns out, I found this fascinating, and so I have followed a path arising from this work ever since. Initially, I was testing an experimental drug – a growth hormone secretagogue that stimulated growth hormone release. It turned out that the drug acts via a novel receptor, and this led to the identification of a natural hormone: ghrelin. I was in the right place at the right time. I do think that luck is something you need in science, alongside hard work.

> *'I want to provide the maximum possible support for endocrinologists, especially during these challenging economic times.'*

From growth hormone, my interest led me to pituitary tumours and their tumourigenesis. The genetic mechanisms underlying these unique lesions later became one of the pivotal topics in my career. Ghrelin also led me down another path, related to the metabolic effect of hormones. After a bumpy start, we had some exciting findings. One of the projects started as an *in vitro* laboratory experiment and, after 14 years of research, led to a clinical trial. I feel privileged to have had the opportunity to see this project through. To start with an idea in basic science and end up with a clinical study is the most exciting aspect of my work!

What attracted you to endocrinology?

I was always interested in endocrinology. In medical school, we had an amazing professor of endocrinology, Professor Edit Gláz, who inspired my interest in the subject, and made me see the logic that is so central to the field. In my first academic role after university, I was tasked with teaching young medical students about the endocrine axis, so I decided to try to breathe some life into this subject for them. I hugely enjoyed this stint of teaching, which became a second wave of my love for endocrinology. I ended up at Barts Endocrine Department, one of the most prominent endocrine units in the world at the time. And I am still here, after 31 years!

What do you hope to achieve as President?

I want to provide the maximum possible support for endocrinologists, especially during these challenging economic times. Key to this will be emphasising the core aims of the Society: to support people who are ambitious, who are early in their careers, and who are interested in making an impact in the clinical, basic science and translational aspects of endocrinology. I want to bring people together for discussions at meetings and training courses, and to provide opportunities to encourage basic science and medical students and trainees to select endocrinology as a discipline. I think these are the absolute key issues which we need to support.

What big challenges face the Society and endocrinology at large?

Endocrinology, as a subject, is so exciting – the science is so beautiful. You can never get bored of it. We need to let people know how wide and varied a subject it is, and to encourage the next generation to specialise in the discipline.

Endocrinology produces well-rounded clinicians, whose training is grounded in both endocrinology and general medicine. This creates doctors who have a reputation as lateral thinkers and problem solvers, figuring out even the most complex patients in a hospital. Ensuring that we protect this reputation of endocrine expertise, and engage and retain endocrinologists, is important for our field, and our Society.

Bringing both endocrine scientists and clinicians into research will also stimulate a continued enthusiasm for the subject. We are seeing a worrying trend of reducing numbers of clinical academics in general, so the Society will need to play its part to keep endocrinology at the forefront, both clinically and academically.

'[Setbacks are] part of the game: you are faced with a roadblock, but that does not need to constitute a failure.'

What are you most proud of in your career?

I am probably most proud of the Fellows whom I have trained, and who have gone on to wonderful clinical or academic careers. I keep in touch with all the Fellows and PhD students I have supervised, and it is lovely to see where their paths have taken them, after being at Barts.

In terms of scientific achievements, there are quite a few of which I am proud. None of them is a showstopper, but I believe they have had an impact, one way or another. My early work on ghrelin resulted in my most highly cited paper – with a medical student as the first author. It is quite a simple paper, but it came out at the right time. Then the data around the hormonal regulation of the metabolic enzyme called AMPK led to the clinical study I mentioned. Identifying the genetic cause of the Irish giants and our work on genetic aspects of pituitary disease are now key aspects of my work. I am excited about some data that we are working on right now, so I feel I have lots of things to look forward to and to be happy about.

Who shaped your career?

Quite a lot of people: I have already mentioned Professors Gláz, Besser and Trainer, but most importantly Professor Ashley Grossman. I am really grateful for his incredible mentorship and friendship over the years. Then of course Professor Adrian Clark, who gave me the permanent position where I still am. Of course, my career has very much been shaped by my trainees. Their hard work led to my successes. It is difficult to narrow it down to just a few names; they are like your academic children, and you can never mention your favourite child!

If you had three pieces of advice for aspiring endocrinologists, what would they be?

- First, you need to believe in your ideas – and in yourself. This is the most important. And then push the ideas through. A bit of perseverance is needed sometimes.
- A second piece of advice would be to accept that setbacks are part of academic medicine, and not something that should make you consider changing your career. It is all part of the game: you are faced with a roadblock, but that does not need to constitute a failure. You need to understand that nobody ever receives all the grants they apply for. You hardly ever get your paper accepted without some pushback. (I might even say that, if your paper is easily accepted by a journal, then you did not submit it to the right journal!) You need to continue to believe in your work, to strengthen it, and to keep going.
- Finally, you need to be able to reinvent yourself from time to time. Keep your eyes open, see the links between two questions that others might not see, pick up new ideas from practically anywhere, learn new techniques, be alert. I hope we can create an environment where we can nurture this creativity through a healthier research culture. This is the way to give the best chances for those who are interested in pursuing clinical or academic endocrinology in the future.

How would you choose to spend a Sunday?

If I think of a 'dream Sunday', I would spend it with my family, now including two grandchildren, and would either go walking or swimming.

New for 2023
SOCIETY BITESIZE WEBINARS

We have some exciting news: we're expanding our SfE Online Skills Academy and will be holding new virtual Society Bitesize Webinars.

BITESIZE WEBINARS

These webinars will be delivered in a new format, centred around our members. So what's different?

- They will be shorter (30 minutes), to allow you to access essential information quickly.
- You can influence the topics that are covered, so we can rapidly respond to your training needs.
- These webinars will be delivered in real time, allowing you to discuss topics during the live Q&A, contributing your own experiences and thoughts to the session.

WEBINAR TOPICS

Initially, we will cover key areas relating to 'Clinic transformation', with the aim of expanding into other areas in the future.

To register for individual webinars, head to the Members' Area at **www.endocrinology.org** and look under 'Events'

Suggest a topic for a Bitesize Webinar by emailing us at **members@endocrinology.org**

We will invite clinicians, nurses and NHS management professionals to present topics which will support you in navigating post-pandemic clinics, as well as offering advice and examples of how to work efficiently and effectively.

Topics to date include:

- How to be a consultant in a new era
- Communicating difficult decisions and treatments
- Advice and Guidance, and Patient Initiated Follow-Up (PIFU)
- Digital health and pathways
- Clinic transformation
- Integrated pathways
- Building business cases
- Nurse-led services (for clinicians)
- GP practice and primary to secondary care interface.

We'd love to hear your suggestions for topics that would suit the new format!

Society for Endocrinology

Events and Training 2023

The Society provides a range of training and events every year, designed to support your career and tailored to your needs.

NATIONAL CLINICAL CASES
24 March

THYROID ULTRASOUND
23 April

EMERGING RESEARCH LEADERS
24 April

CLINICAL UPDATE
24–26 April

ENDOCRINE NURSE UPDATE
25–26 April

SfE BES 2023
13–15 November

NATIONAL TRAINING SCHEME FOR THE USE OF RADIOIODINE IN BENIGN THYROID DISEASE
Details coming soon

And our new-look SfE ONLINE SKILLS ACADEMY including Webinars, Bitesize Webinars and Virtual Coffee Chats

Scan the QR code or visit
www.endocrinology.org/events

Recognising and celebrating EXCELLENCE IN ENDOCRINOLOGY

MEET OUR 2023 MEDALLISTS AND AWARDEES

Join us in congratulating the Society for Endocrinology's 2023 Medallists and Awardees! These globally renowned endocrinologists have made significant contributions to advancing research, knowledge and clinical practice in our field.

You can enjoy their plenary lectures at the Society for Endocrinology BES conference in Glasgow on 13–15 November 2023.

DALE MEDAL

Professor John Speakman
Aberdeen, UK

"I was extremely surprised and beyond happy to receive the message that I had been awarded the 2023 Dale Medal. It is great to see this recognition for the work of my group, which is focused on energy balance and its important roles in obesity and ageing. I feel extremely honoured and I am looking forward to the meeting in Glasgow in November and to presenting some of our work.

EUROPEAN MEDAL

Professor Kristina Schoonjans
Lausanne, Switzerland

"I am deeply honoured to receive the 2023 European Medal from the Society for Endocrinology for my work on bile acid signalling. The discovery that bile acids act as endocrine factors has been transformative to many areas of basic and clinical research. My work is the fruit of many years of passionate teamwork, and I am grateful to all my collaborators and colleagues who have contributed to this achievement.

INTERNATIONAL MEDAL

Professor Holly Ingraham
San Francisco, CA, USA

"What a lovely surprise, opening my email and learning that I would be the 2023 International Medallist. This honour was genuinely unexpected. Work from our lab has leveraged curiosity-driven basic science and biological sex to focus on questions highly relevant to women's health. I can't wait to meet others at SfE BES 2023 in Glasgow, and share our newest findings on hormone-responsive nodes in the brain and peripheral tissues.

NIKKI KIEFFER MEDAL

Mr Phillip Yeoh
London, UK

"I am immensely honoured and humbled to receive 2023 Nikki Kieffer Medal from the Society for Endocrinology. The Society has always been supportive of my endocrine nursing journey, and I am so grateful to my dear friend Nikki Kieffer, who helped and mentored me for all those years. Without the support of my colleagues, this would not have been possible.

JUBILEE MEDAL

Professor Stephen Franks
London, UK

"The Society for Endocrinology has been an important part of my scientific life since I started my career in endocrinology, so I feel immensely proud and honoured to be chosen by my peers to give the Jubilee Medal Lecture.

SOCIETY MEDAL

Professor Ewan Pearson
Dundee, UK

"I am delighted to be awarded the Society Medal, which I accept on behalf of my team, past and present, and the many collaborators whom I've worked with over the years. I've worked on genetics and precision medicine in diabetes over the last 25 years and look forward to presenting some of this work in Glasgow later this year.

TRANSATLANTIC MEDAL

Professor Harald Jueppner
Boston, MA, USA

"I am enormously grateful for being selected as recipient of the 2023 Transatlantic Medal, an award that I could not have imagined when I started my professional path. I am fortunate to have met so many outstanding mentors, colleagues and trainees, who helped me become a clinician scientist and who encouraged my pursuit of research collaborations with various European institutions.

STARLING MEDAL

Dr Li Chan
London, UK

"I am very honoured to be awarded this medal and extremely grateful to the Society for Endocrinology for the recognition. No man (or woman) is an island, and I am thankful for the decades of support from many people (at all levels, at work and at home), societies and funders that have allowed me to flourish as a clinician scientist.

Our Teaching Achievement and Outstanding Clinical Practitioner Awards recognise excellence in teaching and in delivering patient care.

TEACHING ACHIEVEMENT AWARD

Dr Alexander Comninos
London, UK

"I am truly honoured and delighted to receive this award from the Society for Endocrinology. I have been surrounded by brilliant educators for many years, and thank them for inspiring me in my own simple efforts to energise and teach in a wide range of settings.

OUTSTANDING CLINICAL PRACTITIONER AWARD

Professor Richard Quinton
Newcastle upon Tyne, UK

"I am enormously privileged and humbled by this award, albeit already feeling slightly nervous as to how I can possibly deliver a talk at SfE BES Glasgow even half as informative, self-reflective and entertaining as Will Drake's 2022 lecture in Harrogate. My first BES meeting was in Bournemouth in 1994, when I distinctly recall feeling out of my depth in terms of knowledge, experience and networking skills, and the future seemed so completely unmapped. I could not have imagined what a fascinating, stimulating and rewarding field endocrinology would prove to be for me, nor how many enduring friendships I would end up making.

Who do you think deserves recognition for their contribution to endocrinology? Nominations are now open! Visit www.endocrinology.org/medals for further details.

Competency Framework for Adult Endocrine Nursing
NEW AND IMPROVED THIRD EDITION

As mentioned in the last issue, following the success of the first and second editions of the Competency Framework for Adult Endocrine Nursing, the Nurse Committee has been working on a third edition. As well as being a published document, this will also be the basis for an innovative new online platform. We include more details of the new developments here.

EXPANDED COVERAGE

The framework was built on the Benner 'Novice to Expert' approach to the stages of clinical competence, incorporating the levels 'Competent', 'Proficient' and 'Expert'. The third edition has expanded to include 'Novice' and 'Advanced Beginner', which will be aimed at healthcare assistants, nursing associates and student nurses.

The new framework further supports career progression by incorporating the four pillars of advanced practice: (a) clinical, (b) leadership and management, (c) research and (d) education.

> "We are so pleased to see the launch of the online interactive educational platform. Going forward, this will provide nurse members with fantastic opportunities in networking, mentorship, career progression and access to nurse competencies and other key resources. We are grateful to the Society and sponsors for making this happen.
> **Louise Breen, Chair, Nurse Committee**

The third edition will provide an even more comprehensive framework for members working in adult endocrine nursing. As well as additional levels of competency, eight new competencies are being added, including conditions such as arginine vasopressin deficiency (AVP-D (DI)), hyperprolactinaemia and obesity.

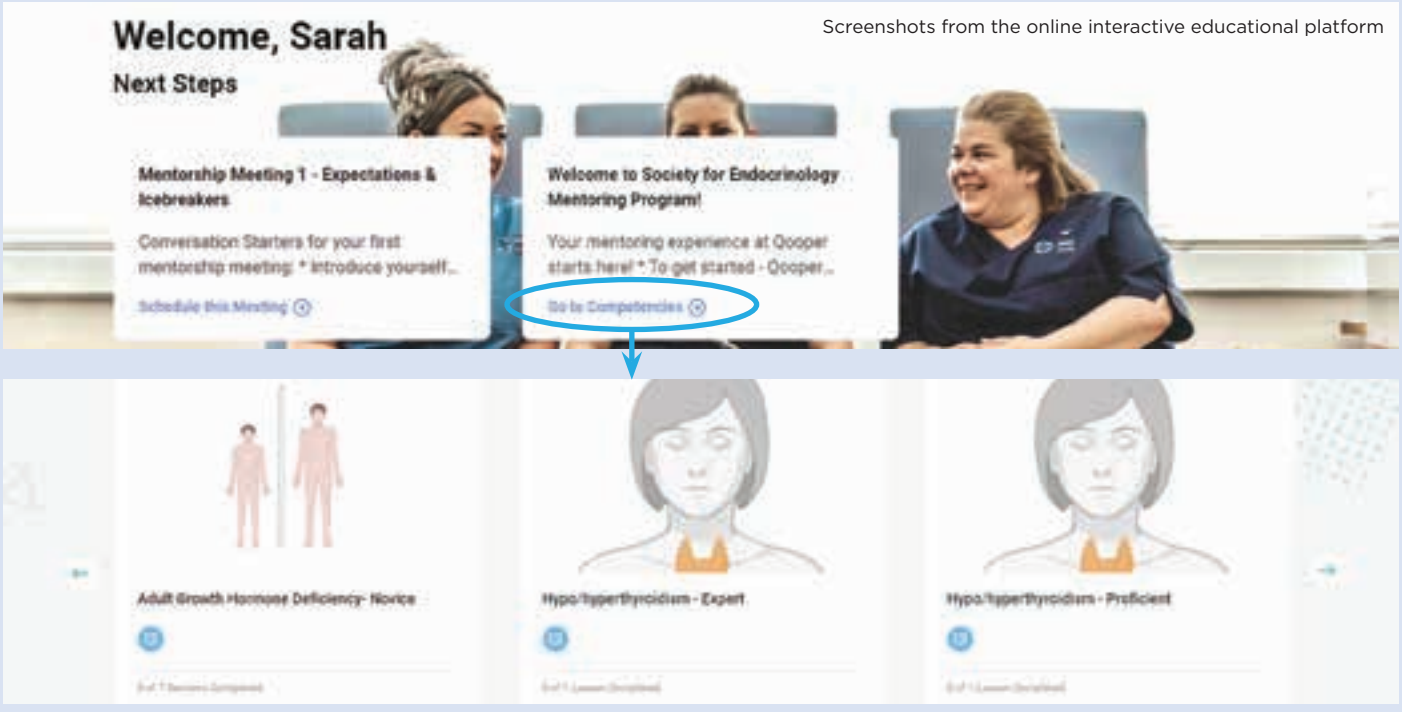
NEW INTERACTIVE PLATFORM

Nurses' feedback on the second edition identified a need for a way of recording their progress, as well as of liaising with more senior nurses for support and guidance. This led to the vision and implementation of an online interactive educational platform. Supported by Sandoz, this new resource is currently being trialled with a small number of nurses.

Not only does this platform allow users to track their progress, it provides links through to multimedia resources and, most importantly, the opportunity to link up with other endocrine nurses anywhere in the UK, through its mentoring network feature.

Once we come to the end of this pilot, we will look to open this up to all our nurse members, whether you are aiming to improve your experience overall or in certain areas, or would like to offer to mentor others. To find out more, or to register your interest, email **nurses@endocrinology.org**.

Screenshots from the online interactive educational platform



Society for Endocrinology

Clinical Resource HUB

Giving you the tools to help transform patient care

This Hub provides the tools you need to help innovate clinical service delivery.

You can find resources such as:

- Patient Initiated Follow-Up (PIFU) guidance
- Job planning
- Clinical pathways
- Patient information sheets
- The full Defining the Future of Endocrinology report and its recommendations

Help us grow this Hub by submitting a resource. Get in touch via clinical@endocrinology.org

SCAN ME

Meet two of your **NEW COMMITTEE MEMBERS**

NIAMH MARTIN
Chair-elect, Public Engagement Committee

Niamh's clinical and research interests include pituitary disease, and she is the Chair of the Imperial Centre for Endocrinology Pituitary Multidisciplinary Service, based at Charing Cross Hospital, London. She leads endocrinology undergraduate education at Imperial College, which she loves.

What inspired you to specialise in endocrinology?
I always loved physiology as an undergraduate, for which endocrinology is a great platform. With hindsight, my intercalated BSc Physiology project focused on exocytosis in adrenal chromaffin cells, so the die was cast early on! More importantly, it was a person who inspired me most; I worked with Professor Karim Meeran in 1998 as his Senior House Officer at the Hammersmith Hospital, London. After that job, I never looked back.

What are you proudest of in your career, so far?
I have managed to keep my faith in the NHS and remain an optimist about its future, despite recent NHS pressures and sometimes negative press. I was involved in acute medicine throughout COVID lockdowns, and I witnessed how amazing all the NHS staff were in the face of such adversity. I felt very proud to be able to be part of that, even though it was often really hard.

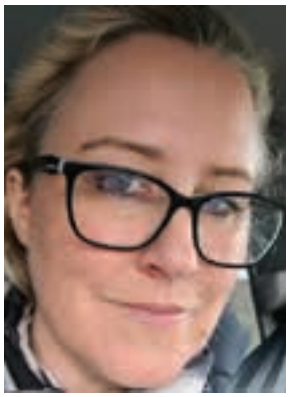
What challenges face endocrinology and the Society?
At the last SfE BES meeting in Harrogate, I was really struck by how tired colleagues are from additional work due to the introduction of Advice and Guidance. This, of course, means clinicians have less time for other valuable activities, such as contributing to the Society for Endocrinology and research. I don't have a solution for this, but I do worry about the implications.

What do you hope to achieve in your new role?
I am looking forward to finding exciting new ways to champion public engagement, particularly showcasing it at future SfE BES conferences.

Why is it good to get involved with Society governance?
I really enjoy meeting endocrinologists from all over the UK and Ireland, to explore how to promote endocrinology. I have met people whom I would never have known otherwise and, for me, that's a huge bonus. It's great to be able to explore different views and ideas as part of an endocrine community. I will also give a shout-out to the Society staff who are wonderful, and so make my governance roles really enjoyable.

What are your words of advice for aspiring endocrinologists?
I have had a wonderful time as an endocrinologist. I am continually challenged and learning more. There are also so many possibilities to subspecialise within endocrinology – I would really recommend it!

KATE WHITE
Nurse Committee Member



Kate is a Registered General Nurse with a background in acute and critical medicine, who has started an endocrine specialty.

She came into nursing as a second career and completed her degree as a clinical support worker.

What inspired you to specialise in endocrinology?
It's funny, I remember when I was doing my degree, sitting in the human anatomy and physiology lessons looking at the endocrine system, thinking, 'Wow that's so complex, shelve that for a later date...' A couple of years ago, I found out that I had an endocrine problem and realised that I had a massive gap in my knowledge. Being a proactive person, I thought that the best way to rectify that was to specialise in it!

What are you proudest of in your career, so far?
This is actually quite a difficult question, but I think it is taking the leap and doing my degree as a mature student. Having been out of academia for a very long time, and starting my degree as a single parent of two children in primary school, it was hard, very hard. But, I'm proud to say I achieved my degree with honours.

What challenges face endocrinology and the Society?
Speaking with colleagues, I think one of the big challenges is raising awareness of endocrine conditions and understanding its management in the hospital setting and in primary care. Ultimately, due to epidemiological factors, endocrine conditions will remain on the increase. The challenge will be for the Society to try and stay ahead of the curve regarding all aspects that feed in to this.

What do you hope to achieve on the Committee?
I would like to think I can help in raising awareness of endocrine conditions and their impact on the individual as a patient in a multitude of environments. I would also like to encourage sharing of information across different formats and platforms.

What inspired you to get involved with Society governance?
It was attending the Society for Endocrinology Nurse Update last year, and knew that I like to put myself in environments where I can learn and improve myself and my knowledge with people from different walks of life. What better way to be involved in governance than in an environment that provides this?

What is your advice to nurses who are considering specialising in endocrinology?
Just go for it. Once you have learnt something, you can take it with you and build on it, no matter what you do or where you go.

Society for Endocrinology

Student Video AWARD

DO YOU TEACH OR SUPERVISE STUDENTS IN SUBJECTS RELATED TO ENDOCRINOLOGY?

Help bring hormones to life and encourage them to apply for the **Student Video Award!**

We're looking for...

Passionate students or postgraduates studying an endocrinology-related topic to submit a 1–2 minute video on the theme 'hormones in the news'

Why apply?

- Win up to £300 and a year of free membership
- Improve science communication skills
- Add a new skill to their CV

Application deadline: **26 April 2023**

Your students can find the previous award winners' videos here

EQUALITY, DIVERSITY AND INCLUSION AT THE SfE BES CONFERENCE

WRITTEN BY DEEPIKA KUMANAN, VICKY SALEM AND KEVIN MURPHY

Opportunities in science and medicine are unequal. Recent years have seen a new and welcome focus on equality, diversity and inclusion across health services and academia, and there has been progress on levelling the playing field, though much remains to do. Understanding where the bias or unfairness lies is important, because it provides an evidence base for interventions to tackle these issues.

Medicine is often classed as a 'feminised' profession, yet women remain underrepresented in clinical academia. Often referred to as the 'leaky pipeline effect', there is still disparity between the proportion of female professionals in junior roles versus senior positions. There has been much research surrounding the causes of female attrition leading to underrepresentation, but fewer studies have identified interventions to reverse it.

Fewer than 20% of clinical professors in the UK are women.[1] There have been a number of initiatives in the UK to improve female retention along academic career pathways, such as the Athena SWAN movement. However, women are still victims of discrepancies in the professional environment. Studies that investigate why fewer women reach professorship found that women tended to have more concerns over work–life balance than their male peers, which negatively impacted their career progression.[2] The pandemic has also led to a greater burden on women due to caregiver responsibilities, leading to greater rates of women dropping out of academic research.[3] With fewer papers published by women during the pandemic, there is a chance that the same career progression of junior female academics will suffer.

OUR WORK SO FAR

Previous pieces by others and ourselves in *The Endocrinologist* have discussed the importance of the visibility, involvement and engagement of members from different genders and ethnicities across the Society. Conferences allow academics to network and raise their profiles, and may therefore be a useful place to introduce interventions that redress gender imbalances. We have described how women were less likely to contribute in discussions after talks at our national annual meeting, the SfE BES conference, in 2017. We found that women asked fewer and shorter questions than men, and had a more empathetic and self-deprecating question style.[4]

At the 2018 conference, an intervention was implemented where more female members were invited to chair sessions, and Chairs were encouraged to open questions to female members when the opportunity presented itself.. This intervention showed promising results, increasing the number of questions from women in 2018.

Building on this work by studying the SfE BES conference 2021 in Edinburgh, we found that, despite a gender-balanced delegacy (54% of delegates were females), women asked fewer questions than men (42.9%), and that the proportion of questions from females increased in the presence of female moderators. Moreover, men used more aggressive and challenging questions than women. These findings were similar to those from the 2017 and 2018 conferences, although it was of note that the gender imbalance in questions was smaller than in previous years.

The proportion of questions from women was nearly equal to those from men in sessions with a female senior Chair and in which the first question was asked by a female, suggesting that increased visibility of women, particularly of higher professional rank, can increase female participation. This is in accordance with work showing that female academic role models aided women in achieving their own professional success, leading to these women publishing more papers and spending time on research.[5]

Differences in the way men and women asked questions persisted. Women more often stated that their question was 'quick' or 'simple' and junior women tended to be more self-deprecating. However, more encouragingly, certain categories of questioning were no longer imbalanced between men and women. This may partly reflect the actions of moderators in trying to open up sessions to a wider range of participants. For example, one Q&A session involved a 'competition' between two Chairs to see who could elicit more questions from trainees.

FUTURE PLANS

This work illustrates the potential impact of simple interventions in increasing the contribution of women in academic conferences. We intend to continue with this work, and are hoping to widen the remit of our studies, investigating, for example, whether the ethnicity of speakers and Chairs has an impact on the demographics of questioners. Evidence suggests that doctors from ethnic minorities are underrepresented in consultant, clinical director and medical director roles, but overrepresented at other grades.[6]

The Society's Equality, Diversity and Inclusion Working Group is currently investigating how we can gather data to understand whether we might need to act to ensure that all of our members are fairly represented and given the opportunity to flourish, and you may have been asked to complete an online survey at SfE BES 2022 about your background and your engagement with the conference.

We hope that, together, this work will help to increase the engagement and visibility of historically underrepresented member groups at the SfE BES conference and, in doing so, make a contribution to bringing down the barriers present in science and academic medicine. You too can make difference. If you attended the conference in 2022 and didn't complete a survey, please log on using the QR code; it only takes a minute. And if you see us approaching you next year to ask some questions, please don't run away…

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